The Efficacy of Prophylactic Transdermal Scopolamine Versus Intravenous Ondansetron on Post Operative Nausea and Vomiting in Patients Undergoing Outpatient Laparoscopic Gynecological Procedures

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Abstract

Postoperative nausea and vomiting is a frequent side effect experienced by patients who have undergone anesthesia. Although years of extensive research have been conducted on prevention and treatment of PONV, there is still an ongoing search for the perfect solution. Experiencing PONV can lead to a multitude of complications, including: decreased patient satisfaction, increased chance of morbidity, increased cost to the patient and hospital, increased workload on recovery staff, and increased length of hospital stay. It is necessary for health care practitioners to be aware of costs and ways to decrease them, avoiding this postoperative complication while utilizing less expensive medications is one mechanism of decreasing the overall cost of providing patient care. The treatment of PONV contains a multitude of options; however, current research indicates the new 5HT-3 receptor antagonists are the most effective treatment choice. Unfortunately, the most effective treatment is currently the most costly option. Research is needed to examine the use of less expensive options, versus the new gold standards, to determine the best choices in the treatment of PONV. The purpose of this study is to examine the effectiveness of **transdermal scopolamine** versus **ondansetron** in the treatment of PONV since scopolamine is significantly cheaper than the newer drug, ondansetron. When determining the "best" available option there is a multitude of factors to consider. These factors include: efficacy, cost, detrimental side effects, benefits, and the safety of the drug. It is the intent of this study to show that scopolamine has equal effectiveness in decreasing the occurrence of PONV with a significant decrease in cost. We also

anticipate a decrease in the incidence of intraoperative bradycardia, pre-operative anxiety, and secretions, with the added benefit of a longer duration of action. These added benefits will thereby make scopolamine a safer, less expensive, and equally as effective alternative to the new 5 HT-3 receptor antagonists. (Key terms are highlighted)

Introduction

The incidence of postoperative nausea and vomiting in patients undergoing laparoscopic gynecological procedures ranges from 50-90%.[15] Despite advances in anesthetic techniques and treatment options, postoperative nausea and vomiting continues to be a significant concern for patients and anesthesia providers. The presence of postoperative nausea and vomiting can lead to several unexpected complications after surgery. Some of the unexpected complications related to postoperative nausea and vomiting can include: increased length of recovery room stay, unanticipated admissions, increased cost of hospitalization, and decreased patient satisfaction.[1,] Studies have shown that one of the biggest fears experienced by patients preoperatively is the fear of being ill.[23] Reducing the incidence of postoperative nausea and vomiting may lead to a decrease in length of hospital stay and therefore decreased cost to the patient and hospital.

There are several factors which contribute to postoperative nausea and vomiting. These factors can be categorized into patient factors, surgical factors, and anesthetic factors.

Mechanism of nausea and vomiting

Nausea is often a precursor to vomiting. This is the conscious awareness of a subconscious excitation in the area of the medulla closely associated with the vomiting center. Causes of nausea can be associated with irritative impulses coming from the gastrointestinal tract, from the lower brain areas associated with motion sickness, or from the cerebral cortex to initiate vomiting. Vomiting can occur without the initial sensation

of nausea, which indicates that not all areas of the vomiting center are associated with the sensation of nausea.[36]

Vomiting is stimulated by the emetic center, an ill-defined area located in the lateral reticular formation of the medulla. This area receives its input from other areas of the brain such as the chemoreceptor trigger zone, vestibular apparatus, cerebellum, solitary tract nucleus, and the higher cortical center.[37] Vagal afferent nerves are the primary peripheral pathways that carry stimuli for nausea and vomiting and transport these impulses to the vomiting center of the brain.[40]

Figure 1: Control mechanisms of vomiting.

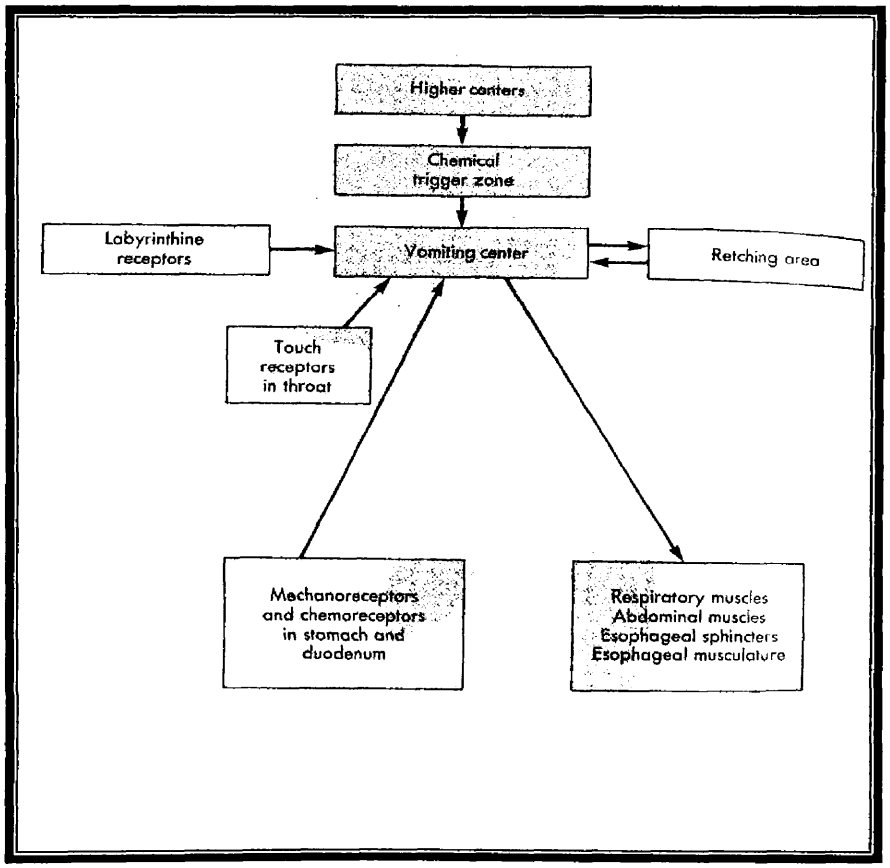


Figure used from Berne et al, Physiology.1998: p. 589-616

Several different receptor sites have also been implicated and include dopamine, acetylcholine/muscarine, histamine, and serotonin (5hydroxytryptamine type 3, 5-HT3) receptors. Receptors for opioids have been found in the chemoreceptor trigger zone, which may attribute to the link between opioids and nausea.[38] The chemoreceptor trigger zone is located on the floor of the fourth ventricle and lies on the blood side of the blood brain barrier and is affected by most blood born substances and chemicals that stimulate vomiting.

Figure 2: Pharmacology of nausea and vomiting.

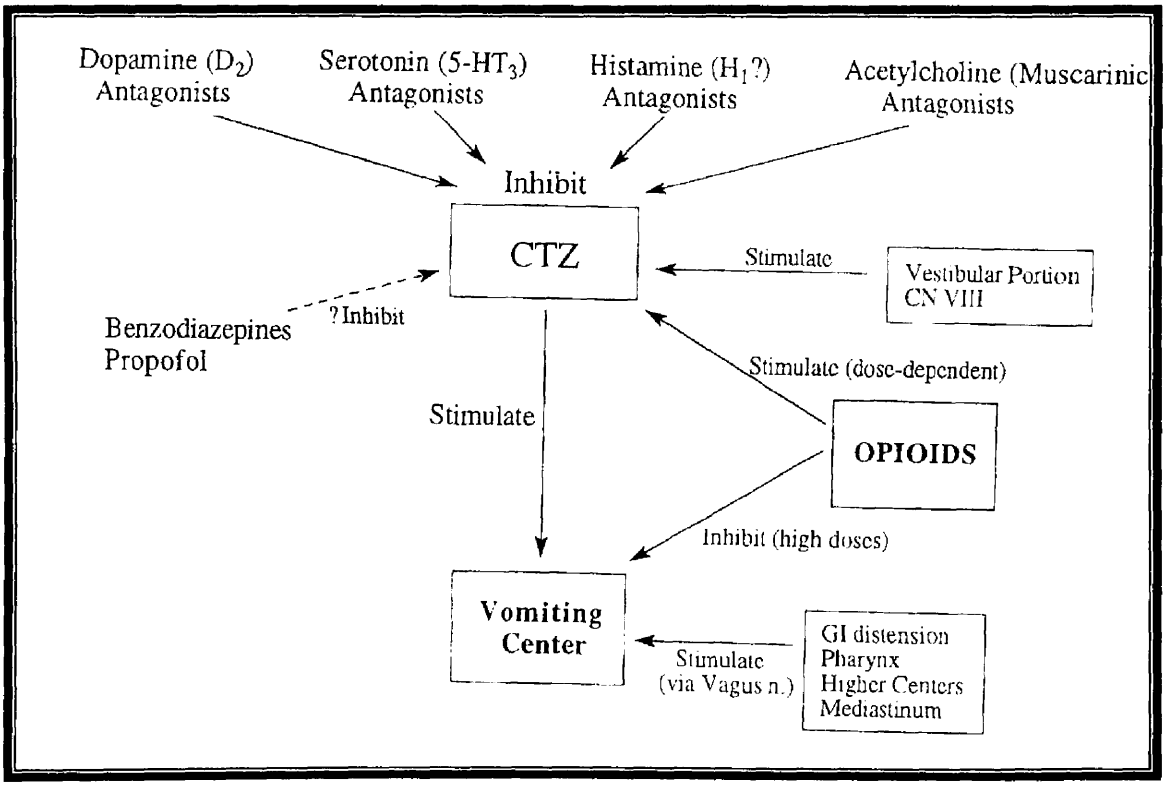


Figure used from Barash et al, Clinical anesthesia. 2001:p. 345-375

Sensory afferent fibers of the trigeminal nerve also terminate in the nucleus tractus solitarius and 5-HT3 receptors are present [41] This may help to explain why surgeries of the head and neck region may be more susceptible to PONV. [40]

When the vomiting center is stimulated, the sequence of events is the same, regardless of the stimulus that initiates the reflex[39]. Vomiting is often preceded by nausea, rapid or irregular heartbeat, dizziness, sweating, pallor, and dilation of the pupils and is the means by which the upper gastrointestinal tract rids itself of gastric contents. Vomiting occurs when all or part of the gastrointestinal tract becomes excited, over distended or irritated. Impulses are transmitted via afferent pathways to the vomiting center, which stimulates motor responses that travel down efferent paths via the 5^{th}, 7^{th}, 9^{th}, 10^{th} and 12^{th} cranial nerves to the upper gastrointestinal tract and spinal nerves to the diaphragm and abdominal muscles.[36]

Stimulation of the vomiting reflex results in a sequence of events that leads up to vomiting. Early in the reflex, reverse peristalsis occurs which pushes gastric contents from the small intestine back into the duodenum. The pyloric sphincter and stomach relax to receive the gastric contents and a forced inspiration then occurs against a closed glottis. This inspiration decreases intra-thoracic pressure while simultaneously increasing intra-abdominal pressure. This forced inspiration is followed by forceful contractions of the abdominal muscles, which sharply increase the intra-abdominal pressures and forces stomach contents into the esophagus. The lower esophageal sphincter relaxes and the antrum and pylorus contract. Rapid propulsion of gastric contents into the esophagus is accompanied by relaxation of the upper esophageal sphincter and the vomitus is projected

into the pharynx and mouth. Entry of vomitus into the trachea is prevented by closure of the vocal cords and glottis, and inhibition of respiration.[39]

Aside from abdominal distention, vomiting can be caused by nervous signals in areas of the brain outside the vomiting center, rapidly changing motions, administration of certain drugs, stimulation of certain areas of the hypothalamus, and various psychic stimuli.[36]

Figure 3: Physiological areas of nausea and vomiting and drugs which affect them

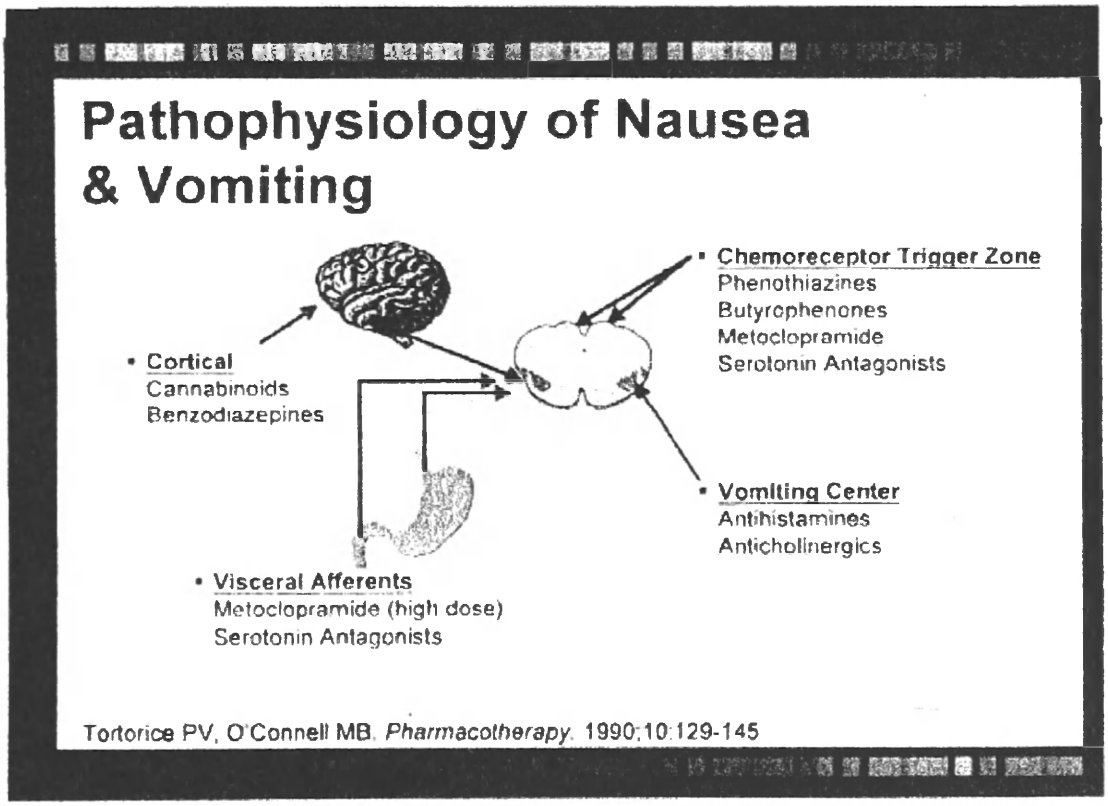


Figure used from Tortorice, et al. Pharmacotherapy. 1990;10:129-145

Understanding the pathophysiology of nausea and vomiting leads to a better knowledge base regarding the occurrence and multiple risk factors contributing to nausea and vomiting.

Patient factors

A multitude of patient risk factors have been identified as contributing to the incidence of PONV. They include: female gender, history of motion sickness or PONV, non-smoking, age, weight, presurgical factors, and degree of postoperative pain.[3,4,6,11]

Gender

Women have a 3-fold increase in the risk of experiencing PONV. In addition, there is an increased risk in patients undergoing general anesthesia near the time of menses, this is thought to be due to circulating E2 estrogen levels.[44, 46]

History of motion sickness or PONV

A positive history of motion sickness or postoperative nausea and vomiting has been shown to be a predictor of increased risk of PONV.[44,45] The explanation may be that these patients have a well developed reflex arc for vomiting.[48]

Non-smoking

Non-smoking has many documented benefits for the surgical patient. However, although it is not clear why, studies have shown that patients who smoke have a significantly decreased risk of PONV.[44,45]

Age

There is evidence that age is a relative factor to the incidence of postoperative nausea and vomiting. A prospective study of 17,638 ambulatory patients by Sinclair, et

al, revealed an increased risk in younger patients.[44,45] The likelihood of PONV decreases 13% per decade of age.[44]

Body weight

There has been a correlation shown between body weight and an increased incidence of PONV. The theories thought to explain this correlation include, the increased amount of adipose tissue acting as a reservoir of anesthetic agents thereby decreasing their rate of elimination in the bloodstream, larger residual gastric volumes, increased incidence of reflux, more gastric inflation during mask ventilation, and the presence of gallbladder and other gastrointestinal disorders.[44,47,48]

Presurgical factors

Preoperative factors which are thought to increase the risk of PONV include: anxiety, starvation, and hypoglycemia.[44] Anxiety is thought to delay gastric emptying and mobility as well as increase gastric volume due to an increase in circulating stress hormones.[49] It is known that patients who have experienced PONV in the past and who are anxious about experiencing again will have an increased chance of its occurrence.[15] It also has been shown that an increase in preoperative anxiety will increase intraoperative anesthetic requirements.[24]

Postoperative pain

Increased postoperative pain has been shown to affect the incidence of postoperative nausea and vomiting. A contributing factor to this is the use of opioids in the management of patients experiencing pain. Opioids have been well documented to contribute to the incidence of PONV.[44]

Surgical factors

Surgical factors which correlate with an increased occurrence of PONV include the type and duration of the surgical procedure as well as the duration of the procedure. Ear-nose-throat, dental procedures, and procedures involving extraocular muscle traction are associated with a high incidence of PONV at 14.3%, followed by orthopedic shoulder procedures and cosmetic surgery. There is also a high incidence with procedures involving middle ear manipulation, peritoneal or intestinal irritation, or testicular traction.[44,50]

In a study by Bellville, et al it was found that the incidence of nausea and vomiting increased 17.5% for anesthesia lasting 30 to 90 minutes. The incidence increased to 46.4% for procedures lasting 150 to 210 minutes. This could be related to the increased amount of opioids used during long procedures, or the effects of prolonged use of other emetic-inducing anesthetic agents.[51]

Anesthetic factors

Effects of anesthetics on the chemotactic center increase the risk of postoperative nausea and vomiting. Swallowed blood or secretions promotes PONV, as does increased gas in the stomach from mask ventilation, nitrous oxide diffusion, or esophageal intubation. A study by Hartung showed that the exclusion of nitrous oxide from an anesthetic reduced the incidence of PONV.[52] The use of regional anesthesia has a decreased incidence of PONV, although the difference narrows once administration of intravenous opioids is needed to control pain. The presence of hypotension due to the sympathetic blockade of regional techniques can also add to the occurrence of PONV.

There is an increased incidence of PONV with the inhalational agents, although not significant, Sevoflurane and Desflurane have been shown to have slightly higher occurrence rates. Of the induction agents, Propofol contributes the least to PONV, followed by barbiturates, then Ketamine and Etomidate. As earlier noted the use of opioids significantly increases the risk of PONV. The use of shorter acting opioids does decrease this risk, however the short duration of analgesia often offsets this effect. There is some evidence that the use of the neuromuscular blockade reversal agent neostigmine, as well as an anticholinergic agent can contribute to PONV.[44]

There has been some noted value of decompression of the stomach contents under anesthesia. Adequate hydration also appears to reduce the incidence of PONV.[44,53] It has been shown that patients who receive higher amounts of IV fluids pre-operatively have a decreased incidence of PONV.[13] Avoiding brisk head movements in the postoperative period also decreases the incidence of PONV, by avoiding vestibular stimulation.[44]

Ondansetron

Recently, ondansetron has become a popular choice for prophylactic and rescue treatment for post operative nausea and vomiting. Zofran® (Ondansetron) is a selective 5-HT3 receptor antagonist.

Mechanism of action

Its mechanism of action has not been fully characterized, however, it is not a dopamine receptor antagonist. Serotonin receptors of the 5-HT3 types are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of

the area postrema. Indications for using a 5-HT3 antagonist include prevention of nausea and vomiting.

Contraindications to use

Contraindications to use include hypersensitivity to ondansetron or hypersensitivity reactions to other selective 5-HT3 receptor antagonists. It should not be used in pregnant or lactating women, and children under 2 years of age.

Side effects

Side effects may include: arrhythmias, bradycardia, EKG alterations, palpitations, syncope, flushing, liver enzyme elevations, and anaphylactic reaction. There can also be redness at the site of injection, hiccups, oculogyric crisis (appearing alone as well as with other dystonic reactions), urticaria, transient blurred vision, and transient dizziness during or shortly after IV infusion.

Toxic dose complications

There is no specific antidote to toxic doses of ondansetron and patients should be managed with supportive therapy. Individual doses as large as 150 mg per day and total daily doses (3 doses) as large as 252 mg have been administered IV without significant adverse effects, despite these doses being more than 10 times the recommended daily dose. In addition to the adverse effects previously listed, the following effects have been described in the setting of ondansetron overdose: sudden blindness of two to three minutes duration, and severe constipation occurred in one patient that was administered 72 mg of ondansetron IV as a single dose. Hypotension (and faintness) occurred in another patient that took 48 mg of oral ondansetron. Following infusion of 32 mg over

only 4 minutes, a vasovagal episode with transient second degree heart block was observed. In all instances, the events resolved completely without morbidity or mortality.[21]

Dosage guidelines/efficacy

There have been a plethora of studies conducted on its efficacy related to several other antiemetics, and in a variety of procedures.[4,6,11,15,16,17,19,25,26,27,28,29,30,31,32,33,34,35] The use of 5HT-3 receptor antagonists have, through extensive research, been shown to be effective with minimal adverse effects.[3] In a study by Kovak et al, it was concluded that ondansetron significantly decreased nausea and emesis scores without causing sedation. It was also found that 4 mg of intravenous ondansetron was the optimal prophylactic dose for female outpatients in the first 24 hours post operatively.[16,17,18] Side effects, as earlier stated, are minimal in respect to the use of ondansetron but can include constipation, dizziness, and headache.[18,20] The therapeutic effects of ondansetron are shown to last for up to 12 hours.[18] In a study by Sniadach et al, it was concluded that 82% of gynecological laparoscopy patients receiving ondansetron experienced no nausea and vomiting.[12]

Treatment costs

It is important to keep in mind the cost of the drugs that are administered to facilitate decreased cost to the patient and to the institution. In a study by Zarate et al, pharmacies and therapeutic committees have shown an increased concern regarding the cost of anti-serotonin drugs, such as prophylactic antiemetics (5-HT3 receptor antagonists).[19] Ondansetron costs approximately $25.65 per dose, and dolasetron

approximately $23.37 per dose, whereas the transdermal scopolamine costs approximately $4.62 per dose.

Scopolamine

Scopolamine hydrobromide (Hyoscine Hydrobromide) is classified as an anticholinergic, antiemetic agent. It also has indications for motion sickness and vertigo and recently has been FDA approved for treatment of PONV.

Mechanism of action

Scopolamine crosses the blood brain barrier and blocks cholinergic stimulation from the vomiting centers of both the vestibular center and the gastrointestinal tract.[10] The transdermal system contains 1.5 mg of scopolamine, which is slowly released at approximately 0.5 mg per day. Each patch consists of four layers for sustained release and the adhesive layer contains a priming dose of scopolamine to achieve therapeutic levels quicker. There are two inactive agents in the patch which are not delivered to the patient; they include mineral oil and polyisobutylene.

Contraindications to use

The use of scopolamine is absolutely contraindicated in patients who are hypersensitive to scopolamine or other belladonna alkaloids and its delivery agents, children, lactating women, and narrow angle glaucoma. It should be used with caution in patients with pyloric, urinary bladder neck, or intestinal obstructions, elderly, impaired liver or kidney function, and history of seizures or psychosis.

Side effects

Side effects may include; dryness of the mouth, drowsiness, blurred vision, pupil dilation, disorientation, delirium, dizziness, restlessness, confusion, memory disturbances, hallucinations, difficulty urinating, skin redness, palpitations, and dry, itchy or reddened eyes.[7] Scopolamine is an anticholinergic agent, which can inhibit the secretion of saliva, decrease gastric secretions and motility, cause drowsiness, and increase heart rate.[7] These anticholinergic actions can all be considered beneficial side effects to the use of scopolamine with anesthesia.

Toxic dose complications

The toxic signs and symptoms for scopolamine include: lethargy, somnolence, coma, confusion, agitation, convulsions, hallucinations, dry, flushed skin, dry mouth, visual disturbances, decreased bowel sounds, urinary retention, tachycardia, hypertension, and supraventricular arrhythmias. Most cases of overdoses can be resolved simply by removal of the patch. More pronounced overdose cases are seen with ingestion of the patch. Treatment includes maintenance of a patent airway, supplemental oxygen, continuous monitoring, and cardiovascular and pulmonary support as needed. If ingested, endoscopic removal of the patch and gastric lavage with administration of activated charcoal are indicated.[7] Although it is not recommended by the physicans' desk reference in treatment of an overdose, other cases of scopolamine overdose have been effectively treated with neostigmine or physostigmine.[7,14]

Dosage guidelines/efficacy

Scopolamine provides some sedation and drowsiness which can help to decrease anxiety pre-operatively and having the patch applied pre-operatively may provide the patient with an increased sense of security that their nausea will be prevented. The decrease in gastric secretions and motility can lead to a decreased risk of nausea and aspiration. The benefits of using the transdermal scopolamine patch also include its relatively inexpensive cost, proven effectiveness in the prevention of PONV, and providing up to 3 days of continuous drug prophylaxis.[10] Research studies regarding the use of transdermal scopolamine for the prevention of PONV have been limited and require further study.[10] Traditionally, scopolamine has been avoided when treating PONV due to its very short duration of action in the parenteral form, however, with the transdermal application its effects can last for up to three days, as previously stated.[12]

Transdermal scopolamine

Transdermal scopolamine, which has historically been used in the treatment of motion sickness, was taken off the market voluntarily in 1994 by its manufacturer because of production problems that could have resulted in lowered effectiveness. Though none of these "less effective" patches were ever released into circulation or used by patients, it was not until 1997 that scopolamine was reinstated by the FDA. During that time, the scopolamine patch underwent process modification, and then endured vigorous testing and inspection before being approved by the FDA for treatment and prevention of PONV.

There have only been a few studies conducted on its efficacy in this arena since its reemergence. In a 2002 meta-analysis by Kranke et al, despite an extensive search, only 23 articles were found related to the use of transdermal scopolamine during 1984-1996.[12] There is a need for current research in this area, due to the reintroduction of scopolamine in 1997. Kranke et al, demonstrated that the use of transdermal scopolamine significantly reduces the risk of experiencing emetic symptoms postoperatively.[12] One study concluded that the use of transdermal scopolamine was effective in reducing PONV in patients who were receiving epidural morphine as postoperative pain control.[8] In a related study, it was also concluded that the use of transdermal scopolamine was effective in decreasing PONV after ear surgery.[9] It is possible that the sole use of the scopolamine patch would result in decrease cost to the patient and institution, while providing equivalent relief of PONV in relationship to ondansetron.

In summary, the mechanism and factors which involve and influence nausea and vomiting are widely varied and complex. Multiple areas involved in the perioperative time period can affect the patients risk of experiencing PONV, these include patient risk factors, surgical risk factors, and anesthetic risk factors. The 5-HT3 receptor antagonists have been shown to be highly effective, however they are currently the most costly prophylactic option. Scopolamine, an anticholinergic agent, offers the potential to be as effective without the high expense.

Definition of terms

Anti-emetic	A medication which prevents or relieves nausea and vomiting
4-2-1 rule	This is a calculation guideline used in anesthesia to determine the amount of fluid replacement a patient requires. The calculation is as follows: 4 mL/kg for the 1st 10 kg, 2 mL/kg for the next 10 kg, then 1 mL/kg for every additional kg over 20 kg. This determines the hourly fluid maintenance required by the patient. This number is also used to calculate the NPO deficit
5-HT3	5-hydroxytryptamine type three, also known as serotonin. A neurotransmitter present in platelets, gastrointestinal mucosa, and mast cells. Thought to be important to neuronal mechanisms involved in sleep and sensory perception
Nausea	Nausea is an unpleasant sensation which usually precedes vomiting.
Ondansetron	Zofran (Ondansetron) is a selective 5-HT3 receptor antagonist, it is used in the prevention and treatment of nausea and vomiting
PONV	Postoperative nausea and vomiting
Scopolamine	Scopolamine hydrobromide (Hyoscine Hydrobromide) is an anticholinergic, antiemetic agent. With indications for treatment of motion sickness, vertigo an PONV.
Vomiting	Vomiting is the ejection of material from the stomach through the mouth

Literature review

Postoperative nausea and vomiting (PONV) is a major concern to patients, and unfortunately there is currently no completely effective preventative treatment that abolishes its occurrence. In a recent study, it was noted that 72% of patients who were surveyed stated that the prevention of PONV should be given highest priority, and that PONV is a great concern to them.[2] Experiencing PONV can cause great distress to patients, as well as causing a heavy workload to recovery room nurses. It is also important to note that a negative anesthesia experience related to nausea and vomiting can influence a patient's attitude toward future experiences with surgery and anesthesia.[11]

The prevention of PONV has been vigorously studied; however, as of yet there is no therapy that has been found to provide 100% relief.[4,6] There have been many recommendations formulated from research on ways to decrease the incidence of PONV. The overall incidence of PONV with all conventional treatments is still 30%, and can increase to as high as 70% in high risk populations.[3] In female patients who undergo gynecological laparoscopic procedures it has been stated that there is an occurrence of PONV in 50% to 90% of patients.[15]

It has been found that the use of multimodal therapy is the most effective in prevention of PONV; however, with the use of new 5-HT3 receptor antagonists the cost of such treatment can be high.[6] In a recent study on the use of multimodal therapy there was a 0% incidence of PONV documented with the combined use of droperidol, dexamethasone, ondansetron, and other methods.[5] As one can conclude the cost of this prophylactic therapy would be inhibitory to most budget conscious institutions. Another

study concluded that prophylaxis is more cost effective then treatment of established PONV.[5] Current trends in prophylaxis for PONV, due to reported adverse side effects of droperidol, have limited the preferred agents to ondansetron, dexamethasone, and dolasetron. Droperidol was given a black box warning by the FDA due to documented cases of sudden cardiac death in high doses associated with its use in psychiatric patients.[22]

Avoiding postoperative nausea and vomiting is a high priority for health care provider and patients. PONV remains a significant problem and can cause many medical risks for the patient. Increased intra-abdominal pressure can jeopardize suture lines in the abdominal, inguinal, or neck area. Increased central venous pressure increases morbidity after ocular, tympanic, or intracranial procedures. There is an increase in the risk of aspiration, especially in the presence of impaired airway reflexes or ability to expel secretions. The sympathetic response to vomiting will increase heart rate and blood pressure, increasing the risk of myocardial ischemia and cardiac dysrhythmias especially in patients with coronary artery disease. Movement due to vomiting can accentuate pain in the postoperative period and accentuate the SNS activation. Gagging and retching can lead to activation of the parasympathetic nervous system inducing hypotension and bradycardia. The presence of PONV delays patient discharge and can necessitate admission of the outpatient surgical patient, thereby reducing patient satisfaction.[44]

Significance and aim

Purpose

Our goal was to determine if there is an equivalent efficacy between the use of transdermal scopolamine and intravenous ondansetron in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic gynecological procedures. The discovery of an equal relationship would significantly impact the cost to patients and hospitals, as well as provide a safer drug choice for patients undergoing this procedure.

Research question

Is prophylactic transdermal scopolamine as effective as intravenous ondansetron in decreasing the incidence of postoperative nausea and vomiting in female patients undergoing outpatient laparoscopic gynecological procedures?

Hypothesis-alternative

Female patients undergoing outpatient gynecological laparoscopic procedures who receive transdermal scopolamine preoperatively will have a decreased incidence of postoperative nausea and vomiting as compared to patients who receive intravenous ondansetron.

Hypothesis-null

There is no difference between the incidence rates of PONV in female patients undergoing gynecological laparoscopic procedures who receive prophylactic transdermal scopolamine versus intravenous ondansetron.

Materials and Methods

Research design

This prospective, single-blinded study, was conducted after institutional review board approval was obtained. Forty three ASA I or II female patients between the ages of 18 to 50, undergoing outpatient laparoscopic gynecological procedures were enrolled in the study. The anesthesia provider was only person aware of which medication (ondansetron vs. transdermal scopolamine) each subject received. Patients, surgeons, and the nurses reporting the PONV were blinded as to group assignments. Exclusion criteria included patients with a history of or those currently experiencing: hypersensitivity to scopolamine or other belladonna alkaloids, hypersensitivity to the delivery agents, ondansetron or other 5-HT3 receptor antagonists, lactating or pregnant women, patients with narrow angle glaucoma, pyloric, urinary bladder neck, or intestinal obstructions, impaired liver or kidney function, or those with a history of seizures or psychosis. Exclusions also included any patient who was currently taking or has taken anticholinergics, antihistamines, or antiemetics within the last five days, or those who have worn a scopolamine patch in the past to prevent subject bias by identification of a placebo versus a medicated patch. (See appendix A). Subjects were also excluded if the laparoscopic procedure was converted to an open procedure or if they were unable to be contacted 24 hours after discharge.

Procedures

Patients were approached on the day of surgery in the outpatient receiving unit by one of three primary investigators. All risks and benefits of participation in the study

were discussed in detail, as well as the purpose for the study. The study consisted of two groups. Envelopes containing group assignments and the individual's identification number were randomly selected by the investigator after informed consent was obtained. The envelope assignments were done in groups of 10 with 5 being group A and 5 being group B, therefore the number of subjects in each group would be equal. Group A received a scopolamine patch preoperatively and a placebo of 2 mL of normal saline on induction. Group B received a placebo patch preoperatively and 2 mL of ondansetron 2mg/mL on induction. The scopolamine or placebo patch was applied to the right postauricular area on admission to the outpatient receiving unit. The goal was to have patch placement at least sixty minutes prior to induction of anesthesia, as recommended by the manufacturer. The time of patch placement was documented on the transdermal scopolamine research flow sheet.(See appendix C) The transdermal scopolamine flow sheet accompanied the patient throughout their hospital stay and was used to document all variables relevant to the study's purpose (see appendix C). The researcher provided the anesthesia caregiver with the patient's kilogram weight, calculated fluid deficit, and anesthesia plan guidelines. The patient was also given information regarding removal of the patch 24 hours post-operatively and discarding it in an appropriate receptacle where it is not within reach of children or pets, as well as proper handwashing after removal. All patients received peripheral IV therapy and replacement of their NPO deficit by the 4-2-1 rule. Patients whose procedures were less than one hour in length received their NPO deficit within that time while longer procedures followed the traditional calculation. Patients were monitored intra-operatively in a standard fashion including: three-lead

electrocardiogram, automatic blood pressure cuff, pulse oximetry, end tidal carbon dioxide, and esophageal stethoscope and temperature. Premedication was achieved with midazolam 1 to 3 mg IV dosed per discretion of the anesthesia provider. Anesthesia was induced with 1 to 5 mcg/kg of fentanyl dosed per discretion of the provider, 1 to 1.5 mg/kg of 2% lidocaine, 2 to 2.5 mg/kg of propofol, and 1 to 1.5 mg/kg of succinylcholine, 0.2 to 0.25 mg/kg of mivacurium, or 0.15 mg/kg of cisatracurium. Anesthesia was maintained with Sevoflurane, Desflurane, or Isoflurane at one MAC or greater, in a 50% oxygen/air combination. Additional muscle relaxation was achieved with either mivacurium or cisatracurium. At the end of the procedure, muscle relaxation was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg, at the discretion of the anesthesia provider. All patients had their stomachs decompressed after induction of anesthesia. No additional antiemetic therapy was provided by the anesthesia provider.

Upon arrival to the recovery room, the patient was immediately assessed by the recovery room nurse and the level of nausea and vomiting was documented on the patient's flow sheet. Nausea was evaluated on a 0 to 3 scale: 0= no nausea, 1= mild nausea, 2= moderate nausea, 3= severe nausea. The number of occurrences of vomiting was also documented, along with any rescue antiemetic therapy given. Rescue therapy was achieved with 4 to 8 mg of ondansetron intravenously. The recovery room nurse also documented any complaints of side effects from the patient on the flow sheet. On discharge form the recovery room, the patient was transferred to the outpatient receiving unit where they where again assessed for levels of nausea, vomiting, and side effects by

the registered nurse. These variables were documented on the patients flow sheet, as well as any antiemetic rescue treatment provided. Each patient was evaluated by a researcher prior to discharge from this unit, and their level of nausea, side effects, and occurrences of vomiting were documented. The patient was instructed to remove the patch after 24 hours. Each patient was contacted by phone 24 hours after their discharge by one of the three primary investigators. An assessment of their level of nausea, occurrences of vomiting, and time of patch removal was documented.

Prior to initiation of the study, each recovery room nurse was instructed on the purpose of the study, the information to be obtained and documented, and toxic effects of the scopolamine patch as well as treatment of a toxic reaction. The nurses in the outpatient receiving unit were also inserviced prior to the initiation of the study, on the purpose of the study, the variables and times to be documented, as well as the toxic effects of scopolamine and its treatment. The primary researcher for the study was available at all times during the study by pager for questions or concerns, as was the primary medical investigator.

Measurement tools

The measurement tool for this study was a data collection sheet called the transdermal scopolamine research flow sheet (see appendix C), which accompanied the patient throughout their hospital stay and was used to record the variables. The pre-operative and post-operative variables were collected by one of the primary investigators. An investigator performed the follow up phone calls, 24 hours after discharge, and recorded data related to the patient's experience post-hospitalization. The intraoperative

information was recorded by the anesthesia provider who was blinded to the group assignment. The recovery room and outpatient receiving unit nurse documented the information during the postoperative time period, and was also blinded to the group assignment.

Statistical Analysis

Descriptive analysis was done to determine mean, range, and standard deviation of interval data including age, weight, and ASA status, comparison of the two groups equivalence in these categories was done by the *t*-test of means. For categorical data, frequency distribution was done. The existence of differences between the groups regarding the mean number of the occurrences of nausea and vomiting was calculated using the independent *t*-test. Differences in the proportions of results between the two drugs was calculated using Chi-square analysis. The level of significance is set at $p<0.05$.

Results

A total of forty-three subjects were enrolled in the study. One subject was excluded due to conversion of the laparoscopic procedure to an open procedure. One subject was excluded by an investigator due to the administration of an antihistamine medication prior to the procedure. Forty-one subjects remained in the analysis. No statistically significant differences where noted in age, weight, ASA classification, time of patch placement to the start of the procedure, administration of an anticholinergic intraoperatively, length of procedure, or length of recovery room time or outpatient receiving unit stay (Table 1).

Table 1. Demographics and study variables

	Scopolamine	Ondansetron
n	20	21
Age (yr)	28 ± 6	31 ± 5
ASA physical status		
I	11	9
II	9	12
Kg weight	72 ± 16	66 ± 15
Time of patch placement to surgery start	95 ± 31	104 ± 55
Pts who received an anticholinergic intraoperatively	11	10
Length of procedure (min)	46 ± 47	54 ± 39
Time in PACU (min)	63 ± 21	59 ± 14
Time in 4C (min)	139 ± 63	108 ± 44

Data are given as mean ± SD or number of patients. No significant difference between groups (P<.05).

The overall incidence of nausea in the study was 63%. In the scopolamine group the incidence of nausea was 55% compared to the 71% incidence in the ondansetron

group The overall occurrence of vomiting was 12%, of the scopolamine subjects the frequency was 20%, whereas the ondansetron subjects had a 5% occurrence. The frequency of adverse side effects between the two groups were statistically insignificant.

Table 5. Incidence of adverse side effects - comparison of groups

Adverse side effect	Scopolamine(n=20)	Ondansetron(n=21)
Dizziness	0	0
Headache	0	0
Dry mouth	10 (50)	6 (29)

Data is given as a number (percentage). No statistical difference between groups (P<.05).

There were no statistical differences in the incidence of nausea between the two groups in the recovery room (Table 2, Graph1), outpatient receiving unit (Table 3, Graph 2), or twenty four hours after discharge (Table 4, Graph 3), (summarized in Graph 4). The overall incidence of vomiting was also similar between the two groups (Table 6, Graph 5). In the scopolamine group a total of 7 (35%) subjects required rescue antiemetic therapy, versus 5 (24%) subjects in the ondansetron group (Table 6).

Table 2. Severity of nausea - recovery room

Severity	Scopolamine(n=20)	Ondansetron(n=21)
None	16 (80)	19 (90)
Mild	2 (10)	2 (9)
Moderate	2 (10)	0
Severe	0	0

Data is given as a number (percentage). No statistical difference between groups (P<.05).

Graph 1. Incidence of nausea in the recovery room

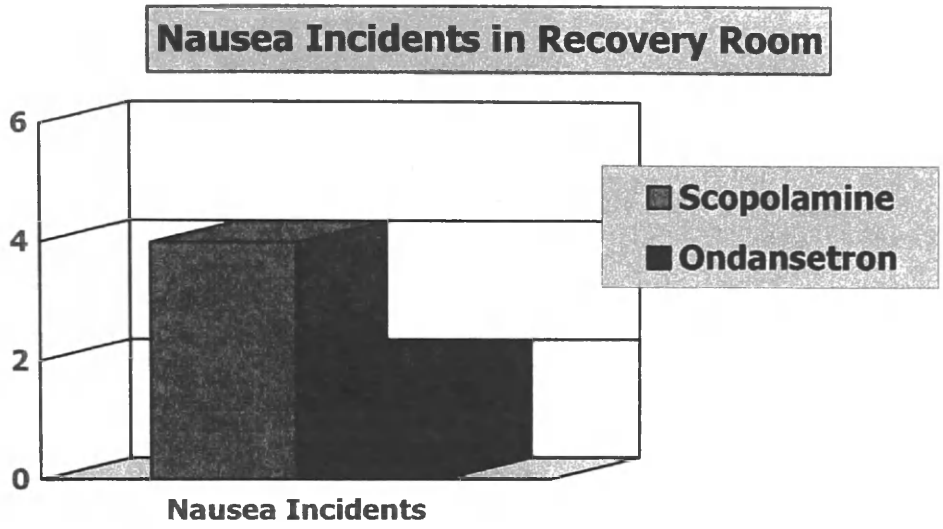


Table 3. Severity of nausea - 4C (Phase II recovery)

Severity	Scopolamine(n=20)	Ondansetron(n=21)
None	15 (75)	15 (71)
Mild	0	2 (9)
Moderate	2 (10)	4 (19)
Severe	3 (15)	0

Data is given as a number (percentage). No statistical difference between groups (P<.05).

Graph 2. Incidence of nausea in 4C

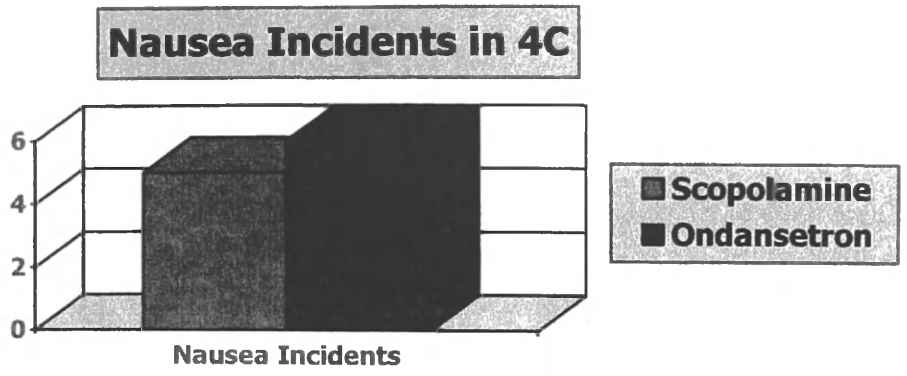
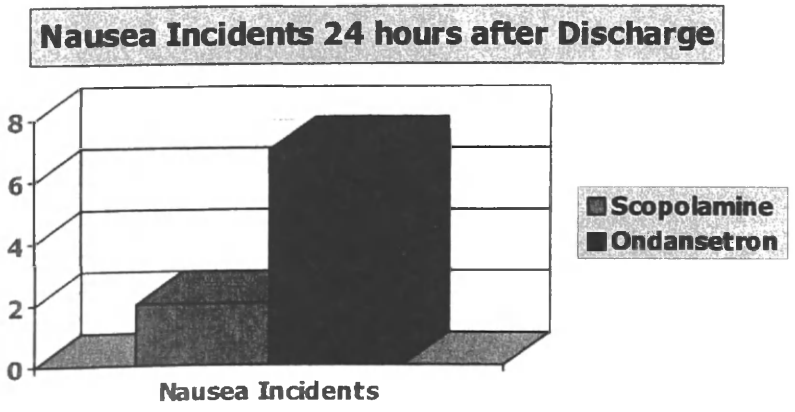


Table 4. Severity of nausea - 24 hours after discharge

Severity	Scopolamine(n=20)	Ondansetron(n=21)
None	18 (90)	14 (67)
Mild	0	2 (9)
Moderate	2 (10)	4 (19)
Severe	0	1 (5)

Data is given as a number (percentage). No statistical difference between groups (P<.05).

Graph 3. Incidence of nausea 24 hours after discharge



Graph 4. Incidence of nausea at all three time frames

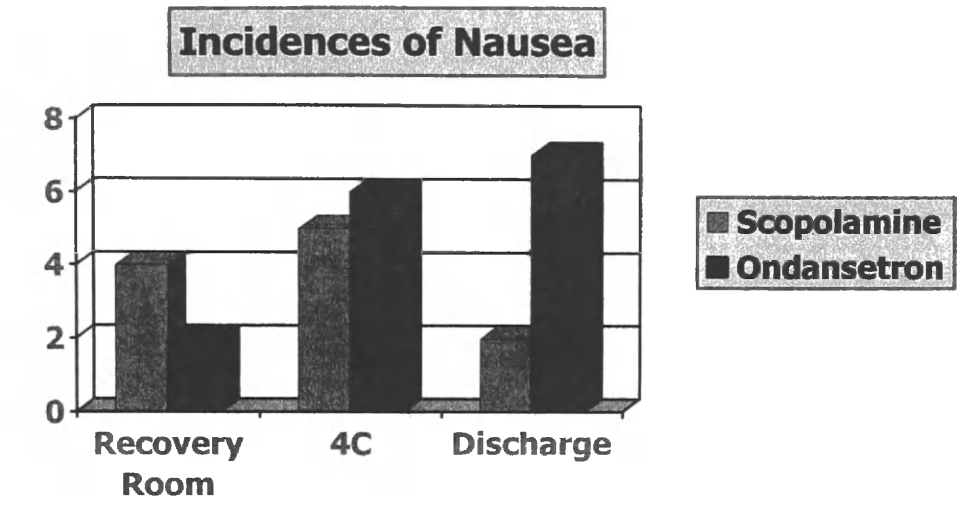
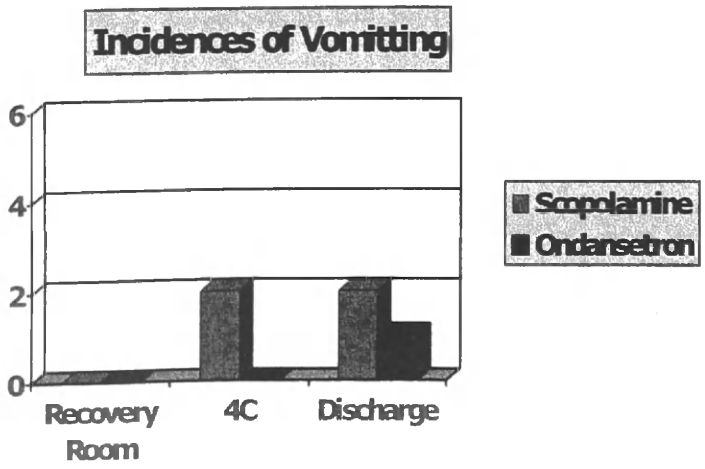


Table 6. Antiemetic rescue treatment – number of subjects

	Scopolamine(n=20)	Ondansetron(n=21)
In PACU	3 (15)	2 (9)
In 4C	4 (20)	3 (14)

Data is given as a number (percentage). No statistical difference between groups (P<.05).

Graph 5. Total incidences of vomiting



Discussion

Our results supported the study's hypothesis that transdermal scopolamine and intravenous ondansetron have an equal efficacy in the prevention of postoperative nausea and vomiting. Though the data analysis showed that there were no dissimilarities in the incidence of nausea and vomiting between the scopolamine and ondansetron patients, we feel that there were developing trends that may have shown statistical significance had there been a larger subject sample group. Immediate postoperative nausea was better controlled in the ondansetron group, however scopolamine was more effective in the later stages of the postoperative period, as demonstrated in graph 4. This result may be supported by considering the onset of action of both drugs, ondansetron is less than ten minutes, whereas the optimal therapeutic effectiveness of transdermal scopolamine can take up to four hours. Combining the average time of preoperative patch placement (approximately 95 minutes) and the average length of the procedure (approximately 46 minutes), the scopolamine patch was only in place for an average time of 2.4 hours prior to admission to the recovery room (Table 1). This time constraint may not have allowed enough time for the patch to reach effective plasma levels, which may explain the decreasing incidence of nausea in the scopolamine subjects as they progressed through the 24 hour postoperative period. Although the duration of action of ondansetron is 12 to 24 hours, we noted an increased incidence of nausea in these subjects after discharge from the recovery room as compared to the subjects who received scopolamine with a duration of action of 72 hours. Although there was a high overall incidence of nausea (63%), the overall occurrence of vomiting was minimal, 12%. Only one patient in the

ondansetron group vomited (5%) compared to four patients in the scopolamine group (20%).

A retrospective review of our study design and methods demonstrated several limitations which may have negatively impacted our overall results. Scopolamine patches could not be placed early enough to reach peak effectiveness prior to the end of the surgical procedure. Intraoperative narcotic amounts were specified, though we were unable to control the amount or type of postoperative narcotic, which could have exacerbated any nausea. The relatively small size of the study groups may have limited our ability to show statistical significance in any of our results. Withholding prophylactic treatment of PONV in high risk populations would be considered unethical, therefore a no-treatment control group was not used.

In the review of previous research, it was noted that a multimodal approach to postoperative nausea and vomiting prevention may be the most effective course of treatment in high risk patients and/or procedures.[5] Laparoscopic gynecological procedures in this age group have consistently demonstrated a high incidence of postoperative nausea and vomiting occurrence. [3,4,6,11,15] A previous study found an overall occurrence of postoperative nausea and vomiting to be 50 to 90% in patients undergoing laparoscopic gynecological procedures. Results of this study concurred, with a finding of 63% occurrence rate.[15] The results of this study demonstrate that a single antiemetic drug was ineffective for preventing nausea and vomiting in this group of high risk patients. These results supported the use of a multimodal treatment approach to these patients. [3,4,6,11]

With the conclusion that transdermal scopolamine is equally effective in the prevention of PONV in patients undergoing gynecological laparoscopic procedures, it is of importance to then consider their cost. Transdermal scopolamine costs approximately $4.62 per patch, whereas 4mg of ondansetron costs approximately $25.65. This results in transdermal scopolamine being a much more cost effective option.

Conclusion

The results of this study demonstrate equal effectiveness between transdermal scopolamine and intravenous ondansetron in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic gynecological procedures. Despite the fact that all of our subjects received an antiemetic treatment prior to surgical incision, there was an unacceptably high overall occurrence rate of nausea (63%) in our study. Therefore, it is the conclusion of the investigators that neither transdermal scopolamine nor intravenous ondansetron alone are the most effective treatment choice for these subjects. Considering that postoperative nausea and vomiting is one of the top concerns of surgical patients, it is disheartening that we had such a high rate of failure of both drugs in preventing nausea.[1,2,11] Though the drugs were given separately preoperatively, perhaps the combination of the increased efficacy of ondansetron in the immediate postoperative period with the delayed onset of scopolamine may have shown more acceptable results. A single modal approach may never be the most effective method of prevention or treatment due to the multiple factors that contribute to nausea and vomiting.

Recommendations

Recommendations for improving the design of this study include; enroll subjects earlier to increase the length of time the patch is in place prior to surgery, and a larger

sample size. A larger patient population may confirm the trends of less nausea in scopolamine patients with increasing postoperative time and less vomiting in ondansetron patients that were found in this study

Future research on the prevention of PONV should include; studies using a combination of scopolamine and ondansetron, earlier patch placement (possibly the night prior to surgery), or higher doses of ondansetron, which may show more positive results then found in this study. It is possible that the combination of scopolamine and ondansetron may result in decreased incidence of PONV for a longer period of time, up to 72 hours. Continued research regarding combination therapy is needed until the treatment modality is found that significantly decreases the incidence of nausea and vomiting in high risk patients.

APPENDIX A

Inclusion and exclusion criteria

Inclusion criteria

Female
ASA category I or II
Age 18-50
Undergoing a laparoscopic gynecological procedure only

Exclusion criteria

Hypersensitivity to scopolamine or other belladonna alkaloids
Hypersensitivity to the delivery agents
Hypersensitivity to ondansetron or other 5-HT3 receptor antagonists
Lactating or pregnant women
Narrow angle glaucoma
Pyloric obstruction
Urinary bladder neck obstruction
Intestinal obstruction
Impaired liver or kidney function
History of seizures or psychosis
Any patient who is currently taking or has taken anticholinergics, antihistamines, or antiemetics within the last five days
Patient refusal of participation
Laparoscopic procedure converting to an open procedure
Inability to contact the subject by phone 24 hours post-operatively
Subjects who have previously worn the transdermal scopolamine patch

APPENDIX B

HURLEY MEDICAL CENTER
PATIENT INFORMATION AND CONSENT FORM

Please read the following material to ensure that you are informed of the nature of this medical research study and how you will participate in it. If you want to take part in this study you should understand the risks and benefits. This consent form provides you with information about the study. Ask the study staff or your doctor to explain any words or information in which you do not understand. Once you have read, understood, and agreed to participate in this study you will be asked to sign this consent form. Federal regulations require written informed consent prior to participation in this medical research study. A copy of the signed consent form will be given to you for your records.

Title: The efficacy of prophylactic transdermal scopolamine versus intravenous ondansetron on postoperative nausea and vomiting in patients undergoing outpatient laparoscopic gynecological procedures.

Introduction and purpose of the study:
You are being invited to take part in a research study to be conducted at Hurley Medical Center. You may be a candidate for this study because you have elected to undergo a laparoscopic gynecological procedure. Procedures of this nature have a high incidence of postoperative nausea and vomiting. Postoperative nausea and vomiting is routinely treated prior to laparoscopic gynecological procedures to decrease the incidence of its occurrence. Your participation in this study is optional, and if you choose not to participate, the standard of care, while being treated at this hospital, will not be affected.

The purpose of the research is to compare the efficacy (desired result) of transdermal (a patch applied to the skin) scopolamine versus intravenous ondansetron, to prevent postoperative nausea and vomiting following laparoscopic gynecological surgery. Scopolamine is an anti-cholinergic, which is widely used to prevention motion sickness and was FDA approved in 1997 for the prevention of postoperative nausea and vomiting. Its effects can last for 3 days if the patch is left in place. Ondansetron is an anti-emetic (prevents and treats vomiting), widely used for prevention and treatment of nausea and vomiting, it also has FDA approval for this use. Its effects last for 12-24 hours.

An estimated 168 patients will participate in the study at Hurley Medical Center. You are asked to take part in this study for two days. If you decide to participate in this study, you will be randomly assigned to one of two groups: scopolamine patch or intravenous ondansetron. No patient will be withheld prophylactic treatment of nausea and vomiting, as is routine practice. A rescue medication will be available, while you are in the hospital, if you do not receive adequate relief from nausea and vomiting after receiving the study drug.

You may be a possible candidate for this research study if:

- You have provided written consent and are capable of reading and understanding the informed consent.
- You are a non-pregnant female between the ages of 18-50, undergoing a laparoscopic gynecological procedure.
- Your medical status, determined at screening, is within the guidelines of this study. This includes the standards of the American Society of Anesthesiologists.

You are not a possible candidate for this research study if:

- Your surgery is an emergency or is for any other reason other than gynecological.
- You are allergic to scopolamine, other belladonna alkaloids, the delivery agents, ondansetron, or other 5-HT3 receptor antagonists.
- You are pregnant or nursing.
- You have narrow angle glaucoma, pyloric obstruction, urinary bladder neck obstruction, intestinal obstruction, impaired liver or kidney function, or a history of seizures or psychosis.
- You are currently, or within the last 5 days, took any anticholinergic, antihistamine, or antiemetic.
- You have, in the opinion of the investigator, any clinically important illness not explicitly excluded by the protocol, a physical or psychological disability, or a laboratory abnormality that might place you at increased risk by being exposed to the medication in this study or which might confound the interpretation of this investigation.
- You are involved in active litigation over disability, compensation, or damages.
- You have an oral temperature over 100.9 degrees F

Study procedure:

After you have decided to participate in this research study, your doctor will make sure you are eligible and the following procedures will be done:

- You will be asked to review the details of your medical history
- You will be examined for eligibility, including your vital signs (heart rate and blood pressure), laboratory results, and if ordered by your physician or the anesthesiologist, electrocardiogram and chest x-ray results.
- You will have a urine pregnancy test, as is standard for all females within your age range undergoing a surgical procedure.

Treatment phase:

Scopolamine and ondansetron are not experimental drugs, both have FDA approval in the treatment and prevention of postoperative nausea and vomiting.

You will be assigned to one of two groups by a process called **randomization**. Randomization means that you are put into a group by chance. The investigator will pull a sealed envelope from a stack to determine which group you will participate in, you have an equal chance of being in either group. Your doctor, his or her staff, clinical monitors or you will not know which treatment you are taking; however this information is available if needed in an emergency. Group A will receive a transdermal scopolamine patch on admission along with a placebo dose of ondansetron at induction of anesthesia, group B will receive a placebo patch on admission and a 4mg intravenous dose of ondansetron at the induction of anesthesia. The placebo is a patch or an injection that

looks like the study drug but contains no active ingredients to prevent or treat your nausea and vomiting. You will be receiving one active drug and one placebo so to avoid bias toward one study drug over the other during the data collection. You will have a small brown patch applied to the back of your right ear after you have consented to participate. You will be asked to leave this patch in place for 24 hours after your surgery. After 24 hours you may remove this patch, discarding it in a receptacle not within reach of children or pets. You should wash your hands thoroughly after removing the patch. You will also receive a medication through your IV at the time of induction of anesthesia, this will be when you are in the operating room. You will be asked questions about your level of nausea once your procedure is completed and you are in the recovery area, data will be recorded regarding occurrences of vomiting. You will also be asked and should report any adverse (bad) reactions you are feeling. These questions will be asked of you in the recovery area, before you are discharged from the hospital, and 24 hours after your surgery. You will be contacted by phone from an investigator. You will also be monitored with an electrocardiogram, blood pressure, and pulse oximetry (measures the level of oxygen concentration in your blood), as standard after surgery.

If you are experiencing nausea or vomiting after receiving the study drugs, you will be allowed to receive other medications while you are in the hospital. The additional drug provided in this study is 4 mg of intravenous ondansetron.

Alternative (other) treatments:

You do not have to take part in this study to receive preventative and/or treatment for your postoperative nausea and vomiting following laparoscopic gynecological surgery. You may choose to receive the standard of care given to laparoscopic, gynecological surgical patients at this hospital.

Risks:

As with any treatment, it is possible the drug you are given could cause adverse (bad) reactions or discomfort.

Drug reactions that may occur related to scopolamine are dryness of the mouth, drowsiness, blurred vision, pupil dilation, disorientation, delirium, restlessness, confusion, memory disturbances, hallucinations, difficulty urinating, skin redness, palpitations, dry, itchy, or reddened eyes.

Drug reactions that may occur related to ondansetron are arrhythmias (irregular heart rhythm) , bradycardia (slow heart rate), electrocardiogram disturbances, palpitations, syncope (passing out), flushing, liver enzyme elevations, allergic reaction, redness at injection site, hiccups, hives, blurred vision, dizziness, constipation, and faintness.

When any intravenous work is performed the needle inserted into the vein may "infiltrate" (become blocked or puncture the wall of the vein it is in) leading to temporary swelling, bruising, bleeding, and/or discomfort.

Benefits:

There is no guarantee that you will receive any medical benefit as a result of participation in this study. However, your participation in the study will contribute information that may benefit other patients. There will be no additional cost to you to take part in this research study beyond the costs of usual medical care you require for laparoscopic gynecological surgical procedures.

Additional information:
If additional side effects of scopolamine or ondansetron are discovered, your doctor will be notified. Any new information about the study drugs that may affect your decision to take part in the study will be given to you.

Voluntary participation and withdrawal
Your decision to take part in this research study is completely voluntary. You may refuse to take part. Even if you choose to take part in this study, you can change your mind anytime and withdraw from the study. Your decision will not affect your medical care, nor will you lose any benefits you might otherwise receive.
For your own safety, if you decide not to continue in this study for any reason, you should notify your study doctor to let him/her know.
Your study doctor may withdraw you from this study without your consent, if he or she feels that it is in your best interest to do so. This may happen if you experience a bad side effect or you do not follow instructions. A full explanation for stopping your participation and possible alternatives will be discussed with you.

Confidentiality
Information collected from you and about you will be treated as confidential (private). Your study doctor and the study investigators will look at your records. Your name will not be used in any information about this study that may be written and published. You will be identified by a special number. By signing this document, you agree (consent) to have the previously mentioned look at your records. Confidentiality of your personal information and information obtained in this study will be maintained by your study doctor and the investigators.

Costs of participating
The administration of medication to prevent nausea and vomiting is a routine practice during laparoscopic gynecological procedures, however it cannot be guaranteed that your insurance company will cover this medication. There is a low risk of increased cost to you above the normal cost of this surgical procedure by participating in this study, since a nausea and vomiting medication would most likely have been given to you even without participation within this study. You, your insurance company, or other third-party payers must pay for all other medicines and/or medical procedures used during the study to treat other medical conditions.

Compensation of research-related injury
If you suffer any medical problem or condition related to the study, have study related questions, or wish to report any study related injury, you must contact

Dr. Mohan Achwal immediately at:
Office: (810) 257-9264
Or pager: (810) 972-3915

Your doctor will see that you receive immediate and necessary care for any study-related injury.
If you are injured as a result of your study participation, you should seek medical help immediately.

If I choose to participate in this study, I will not receive any compensation. I understand that administration of antiemetics is standard and I or my insurance company are responsible for the costs of this routine administration of antiemetic (prevention of nausea and vomiting) medication. In the unlikely event of a physical injury, medical care is available but will be charged to me and/or my insurance company. Hurley Medical Center is not responsible for the cost of this care.

Questions

If you have any questions about this study at any time, you should call your study doctor:
Dr. Mohan Achwal at (810) 257-9264

If you have any questions about your rights as a patient in this study, you may contact the Hurley Medical Center Institutional review Board at (810) 257-9974.

Statement of consent

I, have read (or have had read to me) the information in this consent form. I understand the possible risks and benefits of this study. I have had the opportunity to ask questions and have received satisfactory answers to all my questions.

I am free to withdraw from this study anytime for any reason and that this decision will not affect my future medical care at this facility. I agree to follow the study doctor's instructions. If I feel I have had unexpected or unusual symptoms, I will contact the study doctor at once. By signing this form I do not give up any of the legal rights, which I would otherwise have as a participant in a research study. I will be given a signed and dated copy of this form for my personal records.

I voluntarily consent to take part in this research study.

_____ _____

Signature of patient Date

_____

Print name of patient

_____ _____

Signature of primary investigator Date

_____

Print name of primary investigator

APPENDIX C

TRANSDERMAL SCOPOLAMINE RESEARCH FLOW SHEET

Patient #_____ Date _____ Age_____ ASA_____ Kg_____

Procedure_____

Name of researcher_____

Time of patch placement_____ Time in room_____

Time of procedure's start_____

Time of procedure's end_____

Stomach was decompressed ☐ Yes ☐ No

Time into recovery room_____

Nausea scale: 0= no nausea, 1= mild nausea, 2= moderate nausea, 3= severe nausea

Nausea score on arrival to PACU_____

Patient stated side effects of study drug _____

_____

Rescue antiemetics given _____

Toxic reaction to scopolamine patch ☐ Yes ☐ No

If yes, describe the reaction_____

_____

_____

Treatment for reaction_____

Was the treatment effective ☐ Yes ☐ No If no, describe further treatment provided_____

Time discharged from PACU_____

Nausea score on discharge from PACU_____

Total number of occurrences of vomiting during PACU stay_____

For the researcher to complete:

Medications used for induction_____

_____

_____

_____

Anticholinergic or antiemetic given intra-operatively_____

_____

Nausea score in 4C_____

Antiemetics given in 4C_____

Total number of occurrences of vomiting from admission to 4C until discharge home_____

Time discharged from 4C_____

Patient stated side effects_____

_____

Patient was contacted 24 hours post discharge ☐ **Yes** ☐ **No**

If No, Reason_____

Patients nausea score_____

Total number of occurrences of vomiting from time of discharge until follow up call

_____

Patient stated side effects_____

Time patch was removed_____

References

1. Honkavaara P, Pyykko I. Effects of atropine and scopolamine on bradycardia and emetic symptoms in otoplasty. Laryngoscope 1999;109: 108-12.

2. Kreisler NS, Spiekermann BF, Ascari CM, Rhyne HA, Kloth RL, Sullivan LM, Durieux, ME. Small-dose Droperidol effectively reduces nausea in a general surgical adult patient population. Anesth Analg 2000;91: 1256-61.

3. Tong,G. Postoperative nausea and vomiting- can it be eliminated? JAMA 2002;287:1233-36.

4. Leslie,JB. How can we best prevent or treat postoperative nausea and vomiting? Curr Opin Anaesthesiol 2001;14:623-27.

5.Diemunsch P, Diemunsch AM. Economics of antiemetics. Curr Opin Anaesthesiol 2002;15:233-37.

6. Scuderi PE, James RL, Harris L, Mims GR. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesth Analg 2000;91:1408-14.

7. Transderm scop transdermal therapeutic system. Physicans' desk reference [serial online].Medical economics company.2001 [nine screens].

8. Loper KA, Ready LB, Dorman BH. Prophylactic transdermal scopolamine patches reduce nausea in postoperative patients receiving epidural morphine. Anesth Analg 68:144-46.

9. Reinhart DJ, Klein KW, Schroff E. Transdermal scopolamine for the reduction of postoperative nausea in outpatient ear surgery: a double-blind study, randomized study. Anesth Analg 79:281-84.

10. Bailey PL, Streisand JB, Pace NL, Bubbers SJM, East KA, Mulder S, Stanley TH. Transdermal scopolamine reduces nausea and vomiting after outpatient laparoscopy. Anesthesiology 1990;72:977-80.

11. Sniadach MS, Alberts MS. A comparison of the prophylactic antiemetic effect of Ondansetron and Droperidol on patients undergoing gynecologic laparoscopy. Anesth Analg 1997;85:797-800.

12. Kranke P, Morin A, Roewer N, Wulf H, Eberhart L. The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2002;95:133-43.

13. Monti S, Pokorny ME. Preop fluid bolus reduces risk of post op nausea and vomiting: a pilot study. Journal of advanced nursing practice. 2000;4.

14. Elias MAY, Abouleish E. Scopolamine patch can be confusing to the patient and anesthesiologist: a case report. Anesthesiology. 1997;86:743-4.

15. Morgan D. Management of postoperative nausea and vomiting; the role of droperidol, metoclopramide, and ondansetron. P&T news. 1994;14.

16. Kovak A, McKenzie R, O'Connor T, Duncalf D, Angel J, Gratz I, Fagraeus I, McLeskey C, Joslyn AF. Prophylactic intravenous Ondansetron in female outpatients undergoing gynaecological surgery: a multicentre dose-comparison study. European Journal of Anesthesiology. 1992;6:37-47.

17. Lekprasert V, Meesangnil S, Pausawasdi S, Pongravee V. Efficacy of prophylactic Ondansetron in Thai patients undergoing gastrointestinal tract surgery. Med Assoc Thai. 1996;79:382-7.

18. Ruskin KJ, Doyle DJ. Educational synopses in anesthesiology and critical care medicine. Online journal of anesthesiology. 1996;3.

19. Zarate E, Mehernoor FW, White PF, Fanzca, Klein KW, Sa Rego M, Stewart DG. A comparison of the costs and efficacy of Ondansetron versus Dolasetron for antiemetic prophylaxis. Anesth Analg. 2000;90:1352-8.

20. Kovak AL. Prevention and treatment of postoperative nausea and vomiting. Drugs. 2000;59:213-43.

21. Skidmore-Roth L. Nursing Drug Reference. St. Louis: Mosby; 1995.

22. Tong G, White P, Scuderi P, Watcha M, Kovak A. FDA "black box" warning regarding use of droperidol for postoperative nausea and vomiting: is it justified? Anesthesiology. 2002;97:287-89.

23. Kindler CH, Harms C, Amsler F, Ihde-Scholl T, Scheidegger D. The visual analog scale allows effective measurement of preoperative anxiety and detection of patients' concerns. Anesth Analg 2000;90:706-12.

24. Maranets I, Kain ZN. Preoperative anxiety and intraoperative anesthetic requirements. Anesth Analg 1999;89:1346.

25. Khalil SN, Kataria B, Pearson K, Conahan T, Kallar S, Zahl K, Gillies B, Campbell C, Brahen N, Gilmour I. Ondansetron prevents postoperative nausea and vomiting in women outpatients. Anesth Analg 1994;79:845-851.

26.Cox F. Systematic review of ondansetron for the prevention and treatment of postoperative nausea and vomiting in adults. British journal of theatre nursing 1999;9:556-566.

27.Jokela RM, Kangas-Saarela TA, Valanne VI, Koivuranta MK, Ranta PO, Alahuhta SM. Postoperative nausea and vomiting after Sevoflurane with or without ondansetron compared with Propofol in female patients undergoing breast surgery. Anesth Analg 2000;91:1062-65.

28.Bodner M, White PF. Antiemetic efficacy of ondansetron after outpatient laparoscopy. Anesth Analg 2000;91:1408-14.

29. Moens P, Levarlet M, Hendrickx P, DeGuchteneere E. Single IV bolus dose of ondansetron in the prevention of postoperative nausea and emesis. Acta Anaesthesiol Belg 1997;48:245-50.

30. Helmers JH, Briggs L, Abrahamsson J, Soni J, Moodley J, Forrler M, Hellstern K. A single IV dose of ondansetron 8 mg prior to the induction of anaesthesia reduces postoperative nausea and vomiting in gynaecological patients. Can J Anaesth 1993;40:1155-61.

31. McKenzie R, Sharifi-Azad S, Dershwitz M, Miguel R, Joslyn AF, Tantisira B, Rosenblum F, Rosow CE, Downs JB, Bowie JR, et al. A randomized, double-blind pilot study examining the use of intravenous ondansetron in the prevention of postoperative nausea and vomiting in female inpatients. J Clin Anesth 1993;5:30-6.

32. Rung GW, Claybon A, Hord A, Patel C, Kallgren M, Koppel J, Benedetti C, Creed M, Asgharian A, Bryson J. Intravenous ondansetron for postsurgical opioid-induced nausea and vomiting. Anesth Analg 72:751-55.

33. Leeser J, Lip H. Prevention of postoperative nausea and vomiting using ondansetron, a new, selective, 5-HT3 receptor antagonist. Anesth Analg 58:396-400.

34. Domino KB, Anderson EA, Polissar NL, Posner KL. Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. Anesth Analg 1997; 84:832-38.

35. Fabling JM, Gan TJ, El-Moalem HE, Warner DS, Borel CO. A randomized, double-blinded comparison of ondansetron, droperidol, and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. Anesth Analg 2000;90:186.

36. Guyton, AC, Hall JE. Textbook of Medical Physiology, 9th ed. Saunders, Philadelphia. 1996.

37. Watcha MF, White PF. Postoperative Nausea and Vomiting: Its Etiology, Treatment, and Prevention [review]. Anesthesiology. 1992; 77: 162-184.

38. Rose JB, Watcha MF. Postoperative nausea and vomiting in paediatric patients. Br J Anaesthesiology. 1999; 83: 104-117

39. Berne RM, Levy, MN. Physiology, 4th ed. Mosby, Philadelphia, 1998. p. 589-616

40. Davis CJ, Lake-Baakar GV. Grahame-Smith DG editors. Nausea and Vomiting Mechanisms and Treatment. Berlin: Springer Verlag. 1986

41. Barnes JM. Barnes NM. Costall B. Naylor I. Naylor RJ. Rudd JA. Topographical distribution of 5-HT_3 receptor sites in the ferret brain stem. Naunym-Schmiedebergs Archives of Pharmacology. 1990:38:667-673.

42. Tortorice PV, O'Connell MB. Pharmacotherapy. 1990;10:129-45.

43. Coda BA. Opioids. In:Barash PG, Cullen BF, Stoelting RK, editors. Clinical Anesthesia. 4th ed. Philadelphia: Lippincott, Williams and Wilkins;2001. p. 345-375.

44. Mecca, RS. Postoperative recovery. In: Barash PG, Cullen BF, Stoelting RK, editors. Clinical Anesthesia. 4th ed. Philadelphia: Lippincott, Williams and Wilkins;2001. p. 1377-1402.

45. Sinclair DR, Chung F, Mezei G : Can postoperative nausea and vomiting be predicted? Anesthesiology 91:109, 1999.

46. Beattie WS, Lindblad T, Buckley DN, et al: Menstruation increases the risk of nausea and vomiting after laparoscopy: A prospective, randomized study. Anesthesiology 78:272, 1993.

47. Watch MF, White PF. Postoperative nausea and vomiting. It's etiology, treatment, and prevention. Anesthesiology. 1992:77:162-184.

48. Palazzo MGA, Strunin L. Anesthesia and emesis. Part I: etiology. Canadian Anaesthetists Society journal. 1984:31:178-187.

49. Rabey PG, Smith G. Anaesthetic factors contributing to postoperative nausea and vomiting. British journal of Anaesthesia. 1992:69:40-45.

50. Tramer M, Moore A, McQuay H. Prevention of vomiting after paediatric strabismus surgery: A systematic review using the numbers needed to treat method. Br J Anaesth 75:556:1995

51. Bellville JW, Bross IDJ, Howland WS. Postoperative nausea and vomiting IV: factors related to postoperative nausea and vomiting. Anesthesiology. 1990:21:186-193.

52. Hartung J: Twenty four of twenty seven studies show a greater incidence of emesis associated with nitrous oxide than with alternative anesthetics. Anesth Analg 83:114: 1996.

53. Yogendran S, Kumar B, Cheng D, et al. A prospective, randomized double blinded study of the effect of intravenous fluid therapy on adverse outcomes from outpatient surgery. Anesth Analg 80:682:1995.